

Easy Pathology

— Dr. Abdelrahman Khalifa —

Endocrine System

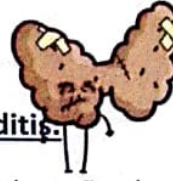


Ain Shams 2017 - 2018

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5 Types **Thyroiditis**

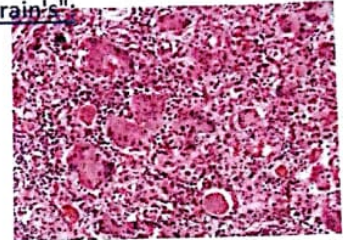


① Acute Infectious thyroiditis:

- Rare, **Suppurative** thyroiditis, due to **Pyogenic** infection or **Fungi**

② Subacute (granulomatous) thyroiditis "De Quervain's"

- Unknown, or due to **viral** infection
- chronic inflammatory cells + **granuloma** with **F.B. giant cells**
- Painful swelling, fever & Transient thyrotoxicosis in some cases



Subacute Lymphocytic

- Uncommon, Autoimmune, infiltrated by **lymphocytes** with **germinal center**
- Transient thyrotoxicosis → **Euthyroid** "Returns Normal"

* V. Imp ② Chronic Hashimoto's thyroiditis:

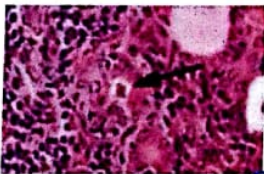
- **Autoimmune**, affecting **middle aged females**, **commonest** cause of **hypothyroidism**
- **Pathogenesis:**

- Genetic (T cell dysregulation) → active **CD8 cytotoxic T cells**
- **CD4** → Interferon gamma → macrophage activation
- **Antibody-mediated**

- **Gross:** Gland is **enlarged** – **pale** - grey "Normally Brownish"

- **Micro:**

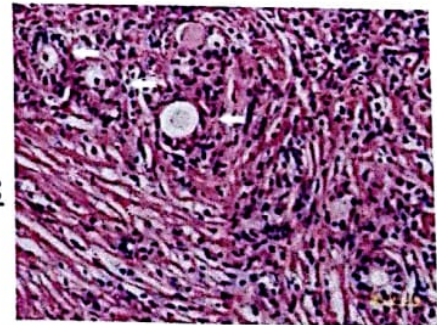
- Atrophic thyroid follicles → **Colloid**.
- **Lymphoid follicles** with germinal centers & plasma cells
- **Hurthle cell (Askanazi)** metaplasia: lined by large, acidophilic, granular cells "OncoCytes"
- Extensive fibrosis (small gland) not common



- **Complications:** Hypothyroidism – Early transient hyperthyroidism

Chronic Reidel's thyroiditis:

- Rare, **Unknown**, with excess **fibrous** tissue formation
- Lymphocytes & plasma cells + **extensive fibrosis**
- Hypothyroidism – **adhesions** (trachea, esophagus, RLN) – mistaken as cancer "Asym. + Firm"



Autoimmune thyroid diseases: Hashimoto – Subacute lymphocytic - Graves

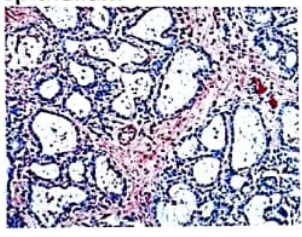
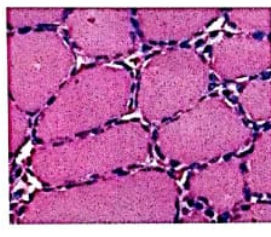
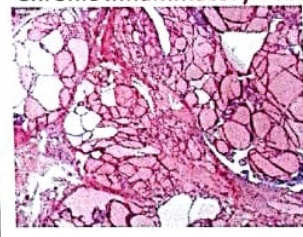
Goiter

Non-inflammatory, non-neoplastic thyroid enlargement



Normal
Hormones level.

Simple Goiter (non toxic)

	Diffuse		Multinodular
	Parenchymatous	Colloid	<i>"Wrong TH" ↑ Iodine Then ↓ Iodine & So on</i>
Aetiology	Iodine deficiency: -Endemic dietary -sporadic in young females or hereditary enzymatic deficiency <i>↓ T₃ & T₄ , ↑ TSH</i> -Diffusely enlarged	adequate iodine supply	Repeated cycles of involution & hyperplasia 
Gross		- Large, Brown , gelatinous	- Nodular – firm -Cut section (necrosis – hemorrhage- calcification)
Micro	-Hyperplasia of thyroid follicles & lining epithelium 	-Distended by colloid Lined by flattened epith. 	-Multiple nodules formed of follicles (variable size) -Separated by fibrous stroma -Chronic inflammatory cells <i>dt Damaged Cells</i> 
Effects	Pressure (Trachea – esophagus-SVC syndrome) – Toxic changes – Malignancy in Multinodular goiter (rare)		

Toxic Goiter 1ry: Grave's or 2ry: complicated simple

Graves disease (1ry Toxic goiter)

Incidence: females, young age. The commonest cause of thyrotoxicosis

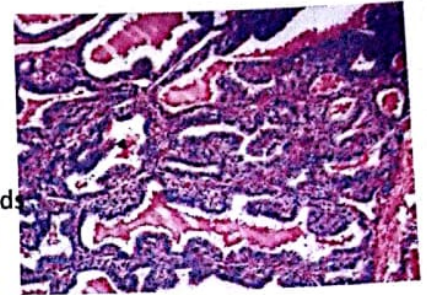
Pathogenesis:

- ↑ Function
- TSI (thyroid stimulating Ig) → Increase T₃, T₄
- TGI (Thyroid growth Ig) → proliferation of thyroid follicles
- TBII (TSH binding inhibitor) *Works As TSI & TGI.*
- T-cell infiltration → **exophthalmus**

Simple Colloid is Bigger
Gross: Diffusely enlarged – Firm – smooth

Micro:

- Proliferated follicles
- Lined with columnar epithelium – hyperplasia and papillary folds
- Containing few colloid (with scalloping) *Peripheral uptake of C.*
- Stroma is vascular + inflammatory cells & lymphoid follicles



Complications:

- **Thyrotoxicosis**
 - Increased BMR → heat intolerance & wet skin
 - Cardiac: Tachy, palpitation, H.F.
 - Nervous, tremors, insomnia
 - GIT: diarrhea, malabsorption, weight loss
 - Eye: Staring gaze, Lid lag
- **Exophthalmus** (retro-orbital fat, edema, lymphoid tissue & ECM)
- **Dermatopathy** (Thick firm skin of chins)
- **Elevated T3, T4, low TSH**



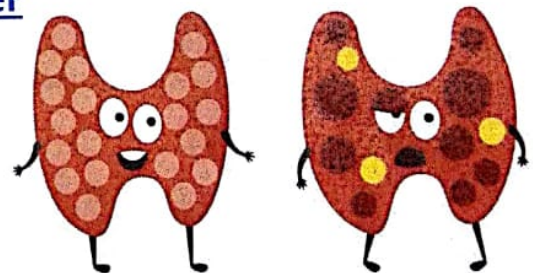
2ry Toxic goiter

Incidence: complicated multinodular goiter

Gross: Large- Nodular – Firm

Micro:

- Nodules containing follicles with hyperplasia & papillary formation
- Lined with columnar epithelium
- Containing colloid (with scalloping)



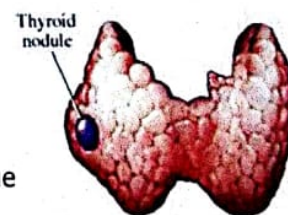
Thyroid adenoma

Gross: Solitary- Rounded – Capsulated – brown

Micro: capsulated with no invasion – compress thyroid tissue

- **Follicular** : forming normal looking follicles (microfollicular – macrofollicular – focal atypia may be seen)
- **Hurthle cell** adenoma (cords of large acidophilic granular cells)

C/P: Silent Cold nodule (inactive) – Toxic symptoms - compression



Hypothyroidism



- **Critinism (infantile or childhood)**

- Congenital
- Fibrotic gland

Mental & physical retardation – protruded tongue – Short body & arms – atrophic sex organs

- **Myxoedema (adult)**

- 1ry: (Hashimoto – Surgical – Dietary cause)
- 2ry: Pituitary causes (low TSH)

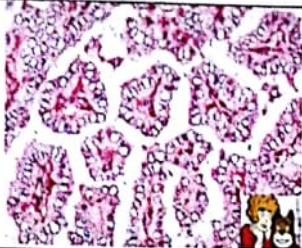
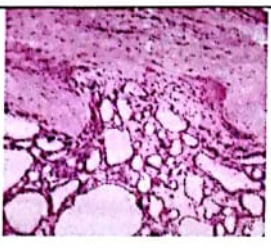
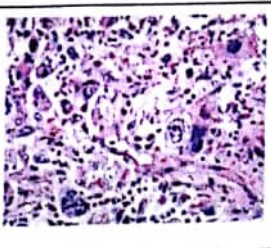
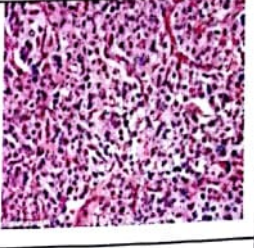
Obese & hyperlipidemia – Dry skin – low BMR ...etc.

cold Intolerance / Hair loss.

** Imp?*

Thyroid carcinoma

	Papillary	Follicular	Anaplastic	Medullary
Incidence	85% More in females young	10% More in females middle age	1% More in females old age	4%
P.F.	Ionizing <u>radiation</u>	Follicular <u>adenoma</u> Multinodular <u>goiter</u>	---	<u>MEN 2</u> <i>Multiple Endocrine Neoplasia</i>
Origin	Follicular cells	Follicular cells	Follicular cells	<u>C-cells (N/E)</u> <i>ParaFollicular</i>
Gross	<u>capsulated</u> → <u>infiltrative</u> <u>granular C/S</u> <u>Calcifications</u>	<u>capsulated</u> → <u>infiltrative</u> fleshy	Irregular ill defined N/H	Nodules N/H
Micro	- <u>Papillary</u> type: complex papillae - The core contain <u>psammoma bodies</u> - The covering malignant cells show <u>neuclear</u> features: * <u>Optically clear</u> (no nucleoli) – <u>Inclusions – ground glass</u> <u>nucleus – nuclear grooving</u> - <u>Follicular variant</u> : showing follicles, with same nuclear features	- similar to <u>follicular adenoma</u> (crowded glands or sheets) - anaplasia is minimal - diagnosed by <u>invasion</u> (capsular or vascular)	- Highly <u>anaplastic</u> pleomorphic cells - <u>giant cells & spindle cells</u>	- solid sheets or follicles of <u>polygonal</u> or <u>spindle cells</u> - stroma contain localized <u>Amyloidosis</u> (<u>altered calcitonin</u>) Stained with Congo rd

				
Spread	-Direct spread -Extensive <u>lymphatic</u> -rare blood "Cervical LNs"	-Direct spread -Minimal lymphatic - <u>Early blood</u> Vascular Invasion.	-Direct spread -Extensive <u>lymphatic</u> -Early <u>blood</u>	-Direct spread -Minimal lymphatic -Late blood

HyperParathyroidism

- 1ry
 - Hyperplasia (in 4 glands)
 - Adenoma 90% (one large, orange gland)
 - carcinoma 1%
- 2ry to renal failure → increased Phosphate → hypocalcemia → compensatory hyperplasia
- Tertiary (ectopic PTH-like protein) : e.g. Lung Squamous cell carcinoma, RCC

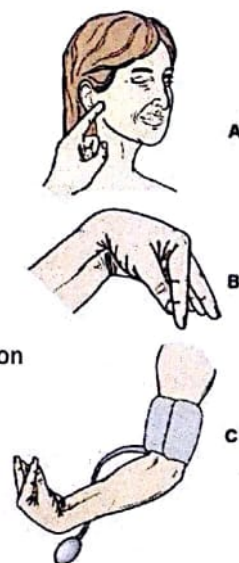


C/P and complications:

- Decalcification of bone → Ostitis fibrosa cystica of bone (brown tumor)
- Metastatic calcification → Renal calcinosis & stones

HypoParathyroidism

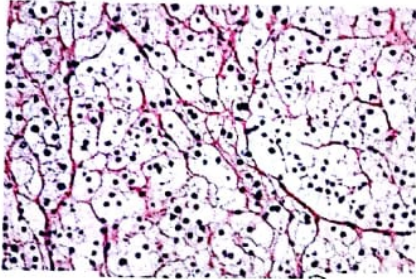
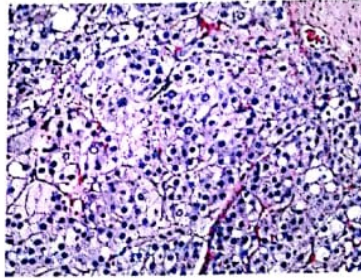
- Congenital hypoplasia or Surgical removal → Hypocalcemia with no effect on Phosphate → tetany



Adrenal Tumors

Cortical Tumors



Adenoma	Adenocarcinoma
Small 1-2 cm Yellowish tan	Large N/H
Micro: Normal cortical cells (with lipid vacuoles) Minimal Atypia 	-Similar to adenoma (differentiated) -Highly Anaplastic (Undifferentiated) 
Asymptomatic or cushing	Spread to adrenal vein & regional L.N. (sure evidence of malignancy)

Medullary Tumors:

1-Pheochromocytoma

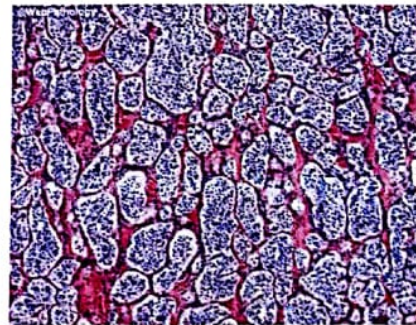
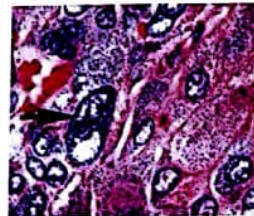
rare, catecholamine-secreting tumor, arising from sympathetic ganglia

Incidence:

10% children, 10% bilateral, 10% extra-adrenal (e.g. carotid body), 10% malignant
10% associated with **MEN**

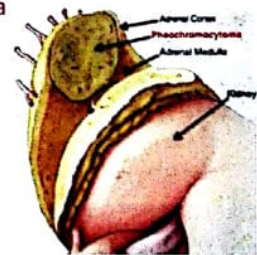
Gross: well defined – not capsulated – yellow - areas of N/H

Micro: solid nests "Zellballen" of Chromaffin cells spindle or polygonal (**granular cytoplasm - Nuclear pleomorphism**). + fibrovascular stroma



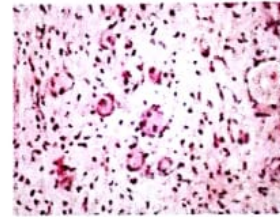
Evidence of malignancy is: metastasis

C/P & complications: Hypertension, high ACTH & somatostatin, VMA in urine



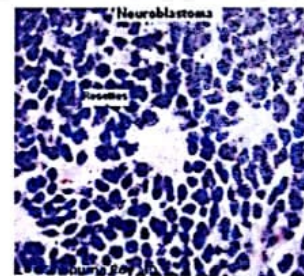
2-Ganglioneuroma

- Benign tumor of Large ganglion cells → compression



3-Neuroblastoma

- The **most common** Embryonic tumor < 6 y
- Origin from embryonic neural cells, Adrenal or extra-adrenal (sympathetic)
- **Gross:** Large – ill defined – N/H
- **Micro:** Small malignant embryonic cells - rounded- dark - with **pseudorosettes**
- **Complications:** secrete catecholamines - Liver metastasis (pepper syndrome)
- **Diagnosis:** Urine sample :
Vanillylmandelic acid **VMA**, Homovallinic acid **HVA**, **dopamine**



Cushing's syndrome

(excess glucocorticoides)

Causes:

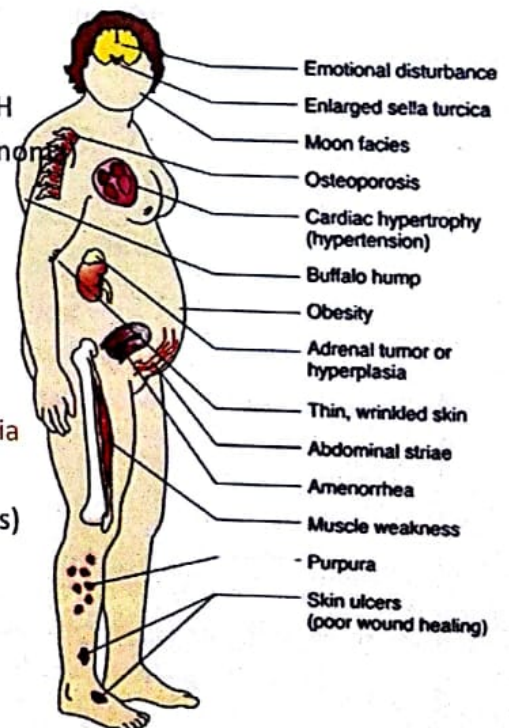
- **Endogenous**
 - Pituitary Adenoma (Basophil cells) 70% → ACTH
 - Adrenal lesions (hyperplasia, adenoma or carcinoma)
 - Ectopic ACTH (e.g. small cell carcinoma)
- **Exogenous**
 - Cortisone intake (long period)

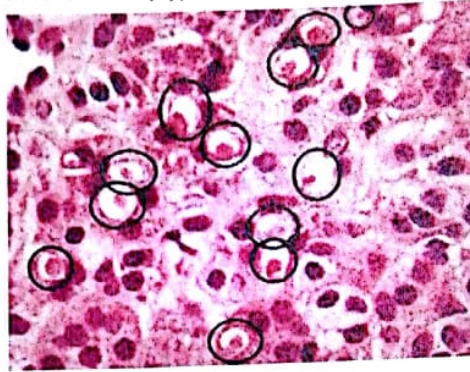
Morphology:

- **Endogenous**
 - In pituitary cause → Adrenal cortical hyperplasia
 - Adrenal adenoma :
small- capsulated – yellow (zona fasciculata cells)
- **Exogenous** Cortisone → cortical atrophy

Clinical:

- More in young females
- Obese – Moon face – weakness – Hypertension – DM- menstrual disorders



Conn's syndrome(Aldosterone-secreting cortical adenoma)**Gross:** Small – Capsulated – yellow**Micro:** **Vacuolated** cells + Cytoplasmic inclusions (**spironolactone** bodies)**Clinical:** Hyperaldosteronism (*Hypertension, Hypokalemia, Polyurea, Albuminurea*)**Adrenogenital syndrome**(Excess androgen)**Causes:**

- Cortical tumor (mainly **carcinoma**)
- **Hyperplasia** (congenital autosomal recessive enzymatic defect), associated with low cortisone & aldosterone

Clinical: boys (Precocious puberty) – Female (Virilism, amenorrhea)**Adrenal Insufficiency**

	Acute	Chronic
causes	-Adrenal necrosis & hemorrhage (meningitis, burns) - Waterhouse-Friderichsen syndrome -Surgical removal -Chronic insufficiency + Stress -Steroid rapid withdrwal	-Autoimmune 70% -Infections (AIDS, fungal, TB) -adrenal Metastatic deposits(lung & breast metastasis)
Clinical	Hypotension → Shock Fever, pain, vomiting, diarrhea	Pigmentation (high ACTH → stimulate melanocytes) <u>no pigmentation in 2ry pituitary causes</u> Fever, pain, vomiting, diarrhea Low Na – High K

Pituitary Adenoma

Types	Functioning (GH, Prolactin, ACTH) - Non functioning
Gross	Rounded- capsulated – or <u>invasive</u> Micro < 1cm - Macro > 1cm
Micro	Sheets, or papillae of <u>polygonal monomorphic cells</u> (Acidophil, Basophil, or chromophobe) – could be erosive <u>Lack of Reticulin</u> framework
Complication	<u>Hypo</u> or <u>Hyper</u> function Compression → <u>visual disturbances</u> Carcinoma is diagnosed by <u>metastasis</u>

	Hyperpituitarism	Hypopituitarism
causes	Hyperplasia - Adenoma	Infantilism Post partum necrosis (Sheehan syndrome)
Effects	- <u>Gigantism</u> (excess proportional growth) - <u>Acromegaly</u> , organomegaly & D.M. - <u>Cushing</u>	In infantilism: arrested <u>growth</u> , <u>hypogonadism</u> Sheehan: <u>Myxedema</u> & <u>hypogonadism</u>

Multiple Endocrine Neoplasia (MEN)

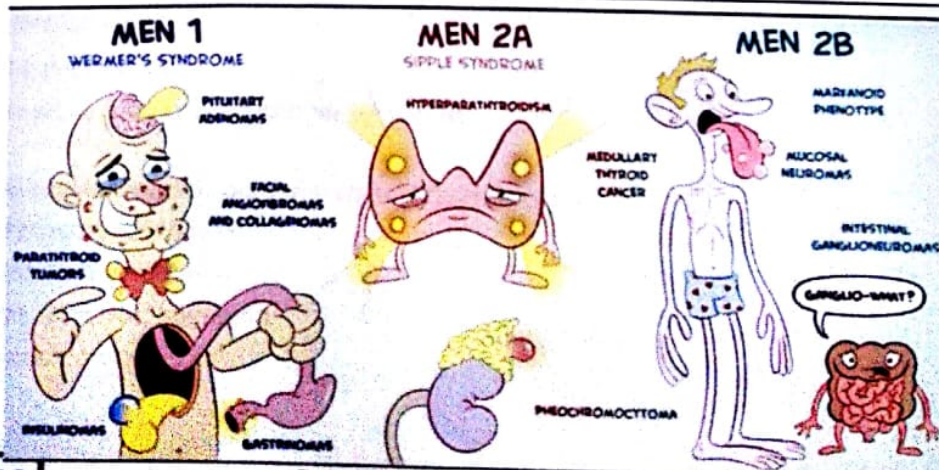
Autosomal dominant diseases characterized by tumors & hyperplasia in different endocrine glands

These tumors are aggressive, recurrent, and multifocal

MEN I : 3 P Pituitary adenoma – Pancreatic adenoma – Parathyroid hyperplasia

MEN II a : Parathyroid hyperplasia – Pheochromocytoma – Medullary thyroid carcinoma

MEN II b Pheochromocytoma – Medullary thyroid carcinoma - Ganglioneurma (subcutaneous), mutation in RET gene.



1. The following type of thyroiditis is characterized by a diffuse fibrosing process:

- a) Infectious thyroiditis
- b) Riedel's thyroiditis
- c) Hashimoto's thyroiditis
- d) Granulomatous thyroiditis

2. Amyloid stroma is characteristic of:

- a) Papillary carcinoma
- b) Follicular carcinoma
- c) Medullary carcinoma
- d) Anaplastic carcinoma

3. Follicular carcinoma is characteristic by all except:

- a) Encapsulated
- b) Psammoma bodies
- c) Formed of follicles of variable size and shape
- d) Capsular and vascular invasion is mandatory to confirm the diagnosis

4. Pituitary carcinoma is diagnosed based on:

- a) Erosion of sella tursica
- b) Microscopic evidence of cellular atypia
- c) Presence of metastasis
- d) Lack of reticulin network

5. Autoimmune thyroid disease include all except:

- a) Hashimoto's thyroiditis
- b) Riedel's thyroiditis
- c) Graves' disease
- d) Lymphocytic thyroiditis

6. Neuroblastoma is characterized by all except:

- a) A tumor of infancy and childhood
- b) Arise from embryonic nerve cells
- c) Homer wright pseudo-rosette
- d) Zellballen nests
- e) Spread to liver causing pepper syndrome

7. Spironolactone bodies are characteristic of:

- a) Parathyroid adenoma
- b) Medullary carcinoma
- c) Adrenocortical adenoma
- d) Pheochromocytoma

8. Causes of cushing syndrome include all the following except:

- a) Adrenal adenoma
- b) Pituitary adenoma
- c) Exogenous intake of glucocorticoids
- d) Bilateral adrenal hemorrhage

9. Pituitary adenoma is characterized by all except:

- a) Functioning or non functioning
- b) The infiltrate is monomorphic
- c) May erode sella tursica
- d) Reticulin staining is strongly positive

10. A 28-year-old female has had difficulty concentrating at work for weeks. She is constantly getting up and walking around to visit coworkers. She complains that the work area is too hot. She seems nervous and spills her coffee a lot. She has been eating more but has lost 5 kg in the past month. Which of the following laboratory findings is most likely to be present:

- a) Decreased plasma insulin
- b) Increased free thyroxine
- c) Decreased iodine uptake
- d) Increased ACTH
- e) Increased calcitonin

11. A 30-year-old female has noted enlargement of her neck over the past few months. On physical examination, she has a diffusely enlarged thyroid that is not painful to palpation. Her TSH level is 0.2 microU/ml. A subtotal thyroidectomy is performed and histologically the tissue shows follicles with papillary infoldings lined by tall columnar cells. These findings are most consistent with:

- a) Subacute granulomatous thyroiditis
- b) Papillary carcinoma
- c) Multinodular goiter
- d) Hashimoto's thyroiditis
- e) Grave's disease

12. A multinodular goiter in a 39 year old female whose thyroid function tests are normal is best characterized by which of the following statements or conditions:

- a. Possible development of thyrotoxicosis
- b. Predisposition to development of papillary carcinoma
- c. Presence of thyroid stimulating immunoglobulins
- d. Previous viral infection
- e. Painful enlargement

13. A 35-year-old female presents with fullness in her neck .She otherwise feels fine and has had no major illnesses. Your physical examination reveals painless symmetric enlargement of the thyroid gland. A complete blood count, electrolyte panel, and urinalysis are all normal. The serum free thyroxine index and TSH are normal. The most likely explanation for these findings is:

- a. Grave's disease
- b. Follicular carcinoma
- c. Simple goiter
- d. Hashimoto's thyroiditis
- e. Pituitary adenoma

14. Dark hemorrhagic and slightly enlarged adrenals were found at autopsy in a teenager who died only hours after presentation to the emergency room with a less than 1-day history of pharyngitis, fever, and severe headache. These findings are most consistent with:

- a. Idiopathic Addison's disease
- b. Metastatic carcinoma
- c. Meningococcal meningitis
- d. Widespread tuberculosis
- e. Pheochromocytoma

15. While bathing her 1-year-old baby, a mother notices that the boy's abdomen seems larger than normal. The baby has not been feeding well lately, and is below the expected weight for his age. She takes the infant to the family physician who palpates a mass lesion in the abdominal region. A CT scan reveals a 5 cm mass in the left retroperitoneum adjacent to the kidney and displacing the kidney. The most probable diagnosis is:

- a. Congenital adrenal hyperplasia
- b. Adrenal adenoma
- c. Pheochromocytoma
- d. Adrenal cortical carcinoma
- e. Neuroblastoma

16. A 22-year-old female complains of vague abdominal colicky pain along with some pain in her extremities. X-Ray on her long bones reveals generalized osteoporosis. She has felt terrible and depressed for several months. Physical examination reveals no major findings. A chest x-ray is normal. A serum chemistry panel reveals a calcium of 138 mg/dl with a serum albumin of 3.9 g/dl and phosphorus of 2.2 mg/dl. What is the most likely cause of her problem:

- a. Metastatic carcinoma
- b. Parathyroid adenoma
- c. Chronic renal failure
- d. Pituitary adenoma
- e. Thyroid carcinoma

17. The appearance of a 2 cm yellow-tan encapsulated cortical mass of the right adrenal most often:

- a. Appears upon withdrawal of exogenous corticosteroid therapy
- b. Occurs following infection with Neisseria meningitides
- c. Results in virilization of prepubertal females
- d. Is detected via testing for increased urinary homovanillic acid
- e. Produces signs and symptoms of Cushing's syndrome

18. A 62-year-old male with back pain and a fracture at the 18 vertebra is found to have hypercalcemia. He has renal troubles due to repeated formations of ureteric stones. Which of the Following diseases is the LEAST likely to have?

- a. Metastatic renal cell carcinoma
- b. Osteitis fibrosa cystica
- c. Osteoporosis
- d. Multiple myeloma
- e. Rickets

19. A 22-year-old female suffers from post partum haemorrhage following delivery of her second child. He gets a normal term male infant. She overcomes this serious complication by strict medical care and blood transfusion. She was unlucky to discover her Failure to lactate her baby. This is probably the result of:

- a. Sheehan's syndrome
- b. Cushing's syndrome
- c. Empty sella syndrome
- d. Syndrome of inappropriate ADH
- e. Simmonds disease.

20. Three days following admission to the hospital for a cerebrovascular accident that is determined by head CT scan to be due to a right parietal infarction, a 66-year-old female develops hypoglycemia, hyponatremia. And hypovolemia. She then becomes hypotensive and then comatose. Which of the following medications was she lacking:

- a. Thyroxine
- b. Vasopressin
- c. Insulin
- d. Estrogen
- e. Hydrocortisone

21. A 34-year-old woman presents with recurrent episodes of severe headaches, palpitations, tachycardia and sweating. Her blood pressure is found to be elevated during one of those episodes. Which of the following is the most common primary site for the origin of the tumor that could produce these clinical signs & symptoms?

- a. Anterior portion of the pituitary gland
- b. Interstitium of the thyroid gland
- c. Medulla of adrenal gland
- d. Superior portion of the hypothalamus
- e. White pulp of the spleen

22. A 22-year-old woman is discovered to have a non-tender thyroid nodule that is found to be a cold nodule on a radioisotope scan. The pathology report from a fine needle aspiration of the nodule describes a follicular neoplasm. the differential of which includes a benign follicular adenoma and a malignant follicular carcinoma. Which is the single best histologic criterion to differentiate between these two neoplasms?

- a. Hyperplasia of follicles
- b. Inspissation of colloid
- c. Invasion into vessels
- d. Number of mitoses
- e. Presence of atypia

23. A 25 year-old man presents because of fullness in his neck. Physical examination finds enlargement of the thyroid gland resulting from the presence of several small masses in both thyroid lobes. These nodules are surgically resected and the pathology report diagnoses it as papillary carcinoma. Which of the following histologic changes is most characteristic of this type of carcinoma?

- a. An amyloid stroma
- b. Bland microfollicles
- c. Extracellular Russell bodies
- d. Neoplastic C cells
- e. Ground glass, grooved nuclei

24. A 35-year-old woman presents with increasing fatigue, slight weight gain and a low-grade fever. Approximately 3 weeks before developing these symptoms she had a 4-day upper respiratory viral infection. At present a physical examination finds a tender enlarged thyroid gland. If a biopsy specimen reveals granulomatous inflammation with giant cells, which of the following is the correct diagnosis?

- a. De Quervain thyroiditis
- b. Graves' disease
- c. Hashimoto's thyroiditis
- d. Mummer disease
- e. Schmidt syndrome

25. A 35-year-old woman has had headaches & worsening renal pain for 3 months. There are no remarkable physical examination findings. On scanning of the neck, she is found to have a mass involving one of her parathyroid glands. An abdominal CT scan suggests extensive nephrocalcinosis along with urinary tract calculi. Which of the following laboratory test findings is most likely to accompany her disease?

- a. Co2 of 30 mmol/L
- b. Phosphorous of 2.2 mg /dl
- c. Uric acid of 15.1mg/dl
- d. Sodium of 121 mmol/L
- e. Calcium of 14.5 mg/dL % (normal 9-11mg)

26. A 29 year-old primigravida has a placenta previa with extensive blood loss and shock during delivery. Following recovery, she is most likely to have which of the following problems?

- a. Cushing's syndrome
- b. Lack of menstrual cycles
- c. Galactorrhoea
- d. Diabetes insipidus

27. An elderly patient undergoes surgery because of a rapidly progressive thyroid mass. The surgical specimen reveals a poorly circumscribed haemorrhagic tumor extending beyond the thyroid. Histologic sections reveal areas of increased vascularity with Prominent spindling, and pleomorphic giant cells. These findings are most consistent with:

- a. Anaplastic carcinoma
- b. Angiosarcoma
- c. Malignant fibrous histiosytoma
- d. Hemangiopericytoma

28. A 42-year-old man presents with Increasing fatigue and occasional headaches. He states that recently he has had to change his shoe size from 9 to 10 and he thinks that his hands & jaw are now larger. Physical examination reveals a prominent forehead & loser jaw. Enlarged tongue & large hands & feet. Initial laboratory examination reveals increased serum glucose. Which of the following is the most likely explanation for his clinical findings? Mention its cause.

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- a. Acromegaly
 - b. Cretinism
 - c. Diabetes
 - d. Gigantism

29. A 37-year-old man presents with a single, firm mass within the thyroid gland. Histologic examination of the mass reveals organoid nests of tumor cells, separated by broad bands of stroma. The latter stains positively with Congo red stain. Which of the following is the most likely diagnosis?

- a. Follicular carcinoma
- b. Papillary carcinoma
- c. Squamous cell carcinoma
- d. Medullary carcinoma
- e. Anaplastic carcinoma

Answers

1.b 2.c 3.d 4.c 5.b 6.d 7.c 8.d 9.d 10.b 11.e 12.a 13.c 14.c 15.e 16.c 17.e 18.e 19.a
20.e 21.a 22.c 23.e 24.a 25.e 26.b 27.a 28.a 29.d
